

Appl. No. 10/764,428  
Amendment dated December 11, 2007

### **REMARKS**

Entry of the foregoing amendments and reconsideration of the claims of the subject application, in light of the following remarks, is respectfully requested.

Claims 26-27, 82-95, and 115 have been cancelled without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of these claims in one or more continuation applications.

Claims 129 and 130 are new and are supported throughout the specification including at page 33, line 24 to page 34, line 6; and page 41, lines 23-33.

Applicants have amended claims 1, 6, 8, 12-15, 19-20, 25, 28-30, 33, 38-44, 50, 52-54, 56-57, 60, 63-64, 67-69, 71, 74, 96, 100-101, 104, 116-118, and 122. Claims 1, 12-13, 19, 25, 38, 39, 42, 50, 52-54, 56-57, 63-64, 71, 74, 104, and 122 have been amended to clarify the claimed subject matter. Claims 6, 8, 14-15, 20, 28-30, 33, 40-41, 43-44, 60, 67-69, 96, 100-101, and 116-118 have been amended to correct claim dependency, provide for proper antecedent basis and for claim language consistency. No new matter enters by way of this amendment.

### **Interview Summary**

Applicants thank Examiner Huynh and her supervisor for the interview conducted on August 20, 2007. We discussed that the method was a method that could be applied to any antibody or antigen binding fragment. Applicants described a specific example based on an antibody heavy chain variable domain sequence from GenBank record 1BEYH. The examiner indicated that the data in the specification was directed to the heavy chain. The examiner suggested that the claims be amended to include active method steps. The examiner also suggested that claims that have specific amino acid positions require a reference sequence. The examiner also suggested that the language of claim 33 was awkward and should be rephrased. Applicants and the Examiner agreed that a supplemental amendment could be submitted in view of the interview.

### **Claim objections**

The examiner objected to 6, 8, 14, 19-21, 25, 29, 33, 42-44, 49, 50, 52-54, 56-57, 60, 63, 64, 67-68, 82, 83, 87, 92, 101, 117, 118, and 122-124. Claims 82, 83, 87, and 92 have been

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cancelled rendering the objection of these claims moot. While not acquiescing to the rejection and solely to expedite prosecution, the remainder of the listed claims has been amended to address the objections. Applicants request withdrawal of the objections.

**Rejections Under 35 U.S.C. § 112, Second Paragraph**

Claims 1-34, 37-61, 63-74, and 82-127 are rejected under 35 U.S.C. § 112, second paragraph, for being indefinite. Claims 26-27, 82-95, and 115 have been cancelled rendering the rejection of these claims moot. Applicants traverse this rejection with respect to the remainder of the listed claims.

While not acquiescing to the rejection and solely to expedite prosecution, the claims have been amended to address the rejection. Applicants request withdrawal of the rejection.

**Rejections under 35 U.S.C. 102 (e)**

The examiner rejected claims 25-31, 33, 36, and 37 under 35 USC 102(e) as anticipated by U.S. Patent No. 6,884,879('879). Applicants respectfully traverse the rejection.

Claimed subject matter is anticipated only if all of the elements of the claim are found in a single prior art reference. "Anticipation requires the presence in a single prior art reference disclosure of each and every element of the claimed invention, arranged as in the claim."

*Lindemann Mashinenfabrik GmbH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1458 (Fed. Cir. 1984); *See also*, MPEP §2131.

Applicants claim 25 is now directed to a method for preparing a humanized antibody or an antigen binding fragment thereof comprising aligning a hypervariable region 1 (HVR1) and/or hypervariable 2 (HVR2) sequence of a variable domain of a non-human monoclonal antibody to corresponding HVR1 and/or HVR2 sequences of human subgroup variable domain consensus sequences, and selecting the human subgroup variable domain consensus sequence that has a HVR1 and/or HVR2 sequence that has the most sequence identity to the HVR1 and/or HVR2 of the variable domain of the non-human antibody; and preparing the humanized antibody or antigen binding fragment by preparing a variable domain comprising at least one framework (FR) sequence from the selected human subgroup variable domain consensus sequence, and the

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HVR1 and/or HVR2 sequence of the non-human antibody, and expressing the humanized antibody or antigen binding fragment in a host cell.

The examiner contends that "The claims are interpreted as a method of preparing a humanized antibody or antigen binding fragment by expressing said humanized antibody or antigen binding fragment thereof in a host cell and recovering the humanized antibody or antigen binding fragment thereof from the host cell. This is because the wherein clause in the independent claims 25 and 71 is not an active step.....". While not acquiescing to this characterization of the claims or the cited reference, Applicants claim 25 now includes active steps such as "aligning a hypervariable region 1 (HVR1) and/or hypervariable 2 (HVR2) sequence of a variable domain of a non-human monoclonal antibody to corresponding HVR1 and/or HVR2 sequences of human subgroup variable domain consensus sequences, and selecting the human subgroup variable domain consensus sequence that has a HVR1 and/or HVR2 sequence that has the most sequence identity to the HVR1 and/or HVR2 of the variable domain of the non-human antibody". Applicants submit that these amendments to the claims address the rejection presented by the examiner. Based on the foregoing, applicants request withdrawal of the 35 USC 102(e) rejection of these claims.

#### **Rejections under 35 U.S.C. 102 (b)**

The examiner rejected claims 25-31, 33, 36-37, and 71-73 under 35 USC 102(b) as anticipated by WO98/45331. Applicants respectfully traverse the rejection.

Claimed subject matter is anticipated only if all of the elements of the claim are found in a single prior art reference. "Anticipation requires the presence in a single prior art reference disclosure of each and every element of the claimed invention, arranged as in the claim."

*Lindemann Mashinenfabrik GmbH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1458 (Fed. Cir. 1984); *See also*, MPEP §2131.

Applicants claim 25 is directed to a method for preparing a humanized antibody or an antigen binding fragment thereof comprising aligning a hypervariable region 1 (HVR1) and/or hypervariable 2 (HVR2) sequence of a variable domain of a non-human monoclonal antibody to corresponding HVR1 and/or HVR2 sequences of human subgroup variable domain consensus sequences, and selecting the human subgroup variable domain consensus sequence that has a

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HVR1 and/or HVR2 sequence that has the most sequence identity to the HVR1 and/or HVR2 of the variable domain of the non-human antibody; and preparing the humanized antibody or antigen binding fragment by preparing a variable domain comprising at least one framework (FR) sequence from the selected human subgroup variable domain consensus sequence, and the HVR1 and/or HVR2 sequence of the non-human antibody, and expressing the humanized antibody or antigen binding fragment in a host cell.

Applicants claim 71 is directed to a method for preparing a humanized antibody or antigen binding fragment, comprising: substituting at least one amino acid position proximal to a cysteine residue that participates in an intrachain variable domain disulfide bond in a variable domain with a different amino acid, wherein the different amino acid is determined by aligning the a hypervariable region 1 (HVR1) and/or hypervariable region 2 (HVR2) sequence of a non-human monoclonal antibody to corresponding HVR1 and/or HVR2 sequences of human subgroup consensus sequences, and selecting the amino acid found at the corresponding position of the human subgroup variable domain consensus sequence that has a HVR1 and/or HVR2 amino acid sequence with the most sequence identity with the HVR1 and/or HVR2 amino acid sequence of the non-human monoclonal antibody as the different amino acid to form a modified variable domain; expressing a humanized antibody or antigen binding fragment comprising the modified variable domain in a host cell; and recovering the humanized antibody or antigen binding fragment from the host cell.

The examiner contends "The claims are interpreted as a method of preparing a humanized antibody or antigen binding fragment by expressing said humanized antibody or antigen binding fragment thereof in a host cell and recovering the humanized antibody or antigen binding fragment thereof from the host cell. This is because the wherein clause in the independent claims 25 and 71 is not an active step....". While not acquiescing to this characterization of the claims or the cited reference, Applicants' claims 25 now includes active steps such as "aligning a hypervariable region 1 (HVR1) and/or hypervariable 2 (HVR2) sequence of a variable domain of a non-human monoclonal antibody to corresponding HVR1 and/or HVR2 sequences of human subgroup variable domain consensus sequences, and selecting the human subgroup variable domain consensus sequence that has a HVR1 and/or HVR2 sequence that has the most sequence identity to the HVR1 and/or HVR2 of the variable domain

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of the non-human antibody". Applicants submit that these amendments to the claim overcome the rejection.

While not acquiescing to this characterization of the claims or the cited reference, Applicants claim 71 also now includes active steps such as "substituting at least one amino acid position proximal to a cys residue that participates in an intrachain variable domain disulfide bond in a variable domain with a different amino acid, wherein the different amino acid is determined by aligning the a hypervariable region 1 (HVR1) and/or hypervariable region 2 (HVR2) sequence of a non-human monoclonal antibody to corresponding HVR1 and/or HVR2 sequences of human subgroup consensus sequences, and selecting the amino acid found at the corresponding position of the human subgroup variable domain consensus sequence that has a HVR1 and/or HVR2 amino acid sequence with the most sequence identity with the HVR1 and/or HVR2 amino acid sequence of the non-human monoclonal antibody as the different amino acid to form a modified variable domain".

Applicants submit that these amendments to the claims address the rejection presented by the examiner. Based on the foregoing, applicants request withdrawal of the 35 USC 102(b) rejection of these claims.

#### Summary

In view of the above amendments and remarks, Applicants respectfully request a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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